

WHAT IS CLAIMED IS:

1. A molecule comprising SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:10, which molecule (a) immunospecifically binds CD40, and (b) comprises one or more substitutions or insertions in primary amino acid sequence relative to native monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110.
2. The molecule of claim 1 comprising the amino acid sequence of SEQ ID NO:2 or the amino acid sequence of SEQ ID NO:7 or the amino acid sequences of both SEQ ID NO:2 and NO:7.
3. The molecule of claim 1 which is an antibody.
4. The molecule of claim 1 which is a fusion protein comprising the amino acid sequence of a second molecule that is not an antibody.
5. The molecule of claim 4 that comprises an amino acid sequence of bryodin (BD1) fused to SEQ ID NO:7 fused to SEQ ID NO:2.
6. The molecule of claim 1 which is an antibody comprising a variable domain of monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110, and a human constant region.
7. The molecule of any one of claims 1-3 which is purified.
8. A purified protein comprising an amino acid sequence that has at least 95% identity to SEQ ID NO:2 or SEQ ID NO:7, which protein (a) immunospecifically binds CD40;

and (b) comprises one or more substitutions or insertions in primary amino acid sequence relative to native monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110.

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9. A purified protein, which protein (a) competes for binding to CD40 with monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110, (b) increases the binding of CD40 ligand to CD40 by at least 45%, and (c) comprises one or more substitutions or insertions in primary amino acid sequence relative to native monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110.

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10. An isolated nucleic acid comprising SEQ ID NO:1, SEQ ID NO:6, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, or SEQ ID NO:15.

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11. An isolated nucleic acid comprising a nucleotide sequence encoding a protein comprising SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:10.

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12. The isolated nucleic acid of claim 11 comprising a nucleotide sequence encoding a protein comprising (a) a heavy chain variable domain of monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110, and (b) a human constant region.

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13. An isolated nucleic acid comprising a nucleotide sequence encoding a protein comprising an amino acid sequence that has at least 95% identity to SEQ ID NO:2 or SEQ ID NO:7.

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14. An isolated nucleic acid comprising a nucleotide sequence encoding a protein, which protein competes for binding to CD40 with monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession

number PTA-110, and which protein increases the binding of CD40 ligand to CD40 by at least 45%.

15. An isolated nucleic acid comprising a nucleotide  
5 sequence encoding a fusion protein, said fusion protein  
comprising an amino acid sequence of bryodin 1 (BD1) fused to  
SEQ ID NO:7 fused to SEQ ID NO:2.

16. An isolated nucleic acid which hybridizes to the  
10 reverse complement of a DNA consisting of a coding DNA  
sequence encoding a protein consisting of an amino acid  
sequence selected from the group consisting of SEQ ID NO:2  
and SEQ ID NO:7, under highly stringent conditions, which  
isolated nucleic acid encodes a protein that  
15 immunospecifically binds CD40.

17. A recombinant cell containing a recombinant nucleic  
acid vector comprising a nucleotide sequence encoding a  
protein, which protein competes for binding to CD40 with  
20 monoclonal antibody S2C6 as secreted by the hybridoma  
deposited with the ATCC and assigned accession number PTA-  
110, and which protein increases the binding of CD40 ligand  
to CD40 by at least 45%.

18. A recombinant cell containing a recombinant nucleic  
25 acid vector comprising SEQ ID NO:1, SEQ ID NO:6, SEQ ID  
NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, or SEQ ID  
NO:15.

19. A method of producing a protein comprising:  
30 (a) growing a cell containing a recombinant  
nucleotide sequence encoding a protein, which  
protein competes for binding to CD40 with  
monoclonal antibody S2C6 as deposited with the  
ATCC and assigned accession number PTA-110,  
35 and which protein increases the binding of

CD40 ligand to CD40 by at least 45%, such that the protein is expressed by the cell; and  
(b) recovering the expressed protein.

- 5 20. A method of producing a protein comprising:  
    (a) growing a cell containing a recombinant nucleotide sequence encoding a protein comprising SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:10, such that a protein encoded by said nucleotide sequence is expressed by the cell; and  
    (b) recovering the expressed protein.
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- 15 21. A pharmaceutical composition comprising:  
    (a) a molecule comprising SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:10, which molecule (i) immunospecifically binds CD40, (ii) increases the binding of CD40 ligand to CD40 by at least 45%, and (iii) comprises one or more substitutions or insertions in primary amino acid sequence relative to native monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110, in an amount effective for the treatment or prevention of cancer; and  
    (b) a pharmaceutically acceptable carrier.
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- 30 22. A pharmaceutical composition comprising:  
    (a) a purified protein, which protein (i) competes for binding to CD40 with monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110, (ii) increases the binding of CD40 ligand to CD40 by at least 45%, and (iii)
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comprises one or more substitutions or insertions in primary amino acid sequence relative to native monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110, in an amount effective for the treatment or prevention of cancer; and

(b) a pharmaceutically acceptable carrier.

23. A pharmaceutical composition comprising:

(a) a molecule comprising SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:10, which molecule (i) immunospecifically binds CD40, (ii) increases the binding of CD40 ligand to CD40 by at least 45%, and (iii) comprises one or more substitutions or insertions in primary amino acid sequence relative to native monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110, in an amount effective for activating or augmenting an immune response; and

(b) a pharmaceutically acceptable carrier.

24. A pharmaceutical composition comprising:

(a) a purified protein, which protein (i) competes for binding to CD40 with monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110, (ii) increases the binding of CD40 ligand to CD40 by at least 45%, and (iii) comprises one or more substitutions or insertions in primary amino acid sequence relative to native monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110,

- in an amount effective for activating or augmenting an immune response; and  
(b) a pharmaceutically acceptable carrier.

5 25. The pharmaceutical composition of any one of claims 21-24 further comprising CD40 ligand.

26. A method for the treatment or prevention of cancer in a subject comprising:

10 administering to the subject an amount of a molecule comprising SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:10, which molecule (i) immunospecifically binds CD40, (ii) increases the binding of CD40  
15 ligand to CD40 by at least 45%, and (iii) comprises one or more substitutions or insertions in primary amino acid sequence relative to native monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110, which amount is effective for the  
20 treatment or prevention of cancer.

27. A method for the treatment or prevention of cancer in a subject comprising:

25 administering to the subject an amount of a purified protein, which protein (i) competes for binding to CD40 with monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110, (ii)  
30 increases the binding of CD40 ligand to CD40 by at least 45%, and (iii) comprises one or more substitutions or insertions in primary amino acid sequence relative to native monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110,  
35 which amount is effective for the treatment or prevention of cancer.

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28. A method for activating or augmenting the immune response of a subject comprising:

administering to the subject an amount of a molecule comprising SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:10, which molecule (i) immunospecifically binds CD40, (ii) increases the binding of CD40 ligand to CD40 by at least 45%, and (iii) comprises one or more substitutions or insertions in primary amino acid sequence relative to native monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110, which amount is such that the immune response of the subject is activated or augmented.

29. A method for activating or augmenting the immune response of a subject comprising:

administering to the subject an amount of a purified protein, which protein (i) competes for binding to CD40 with monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110, (ii) increases the binding of CD40 ligand to CD40 by at least 45%, and (iii) comprises one or more substitutions or insertions in primary amino acid sequence relative to native monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110, which amount is such that the immune response of the subject is activated or augmented.

30. A method for the treatment or prevention of an immune disorder in a subject comprising:

administering to the subject an amount of a molecule comprising SEQ ID NO:2, SEQ ID NO:3, SEQ

# DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below at 201 et seq. underneath my name.

I believe I am the original, first and sole inventor if only one name is listed at 201 below, or an original, first and joint inventor if plural names are listed at 201 et seq. below, of the subject matter which is claimed and for which a patent is sought on the invention entitled

## RECOMBINANT ANTI-CD40 ANTIBODY AND USES THEREOF

and for which a patent application:

- ☒ is attached hereto and includes amendment(s) filed on (if applicable)  
☐ was filed in the United States on as Application No. (for declaration not accompanying application)  
 with amendment(s) filed on (if applicable)  
☐ was filed as PCT international Application No. on and was amended under PCT Article 19 on (if applicable)

I hereby state that I have reviewed and understand the contents of the above identified application, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, §119(a)-(d) of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

EARLIEST FOREIGN APPLICATION(S), IF ANY, FILED PRIOR TO THE FILING DATE OF THE APPLICATION			
APPLICATION NUMBER	COUNTRY	DATE OF FILING (day, month, year)	PRIORITY CLAIMED
			YES <input type="checkbox"/> NO <input type="checkbox"/>
			YES <input type="checkbox"/> NO <input type="checkbox"/>

I hereby claim the benefit under Title 35, United States Code, §119(e) of any United States provisional application(s) listed below.

APPLICATION NUMBER	FILING DATE

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code §112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

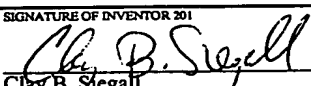
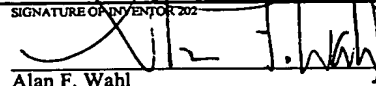
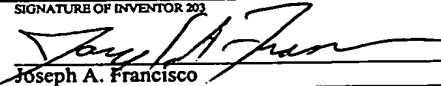
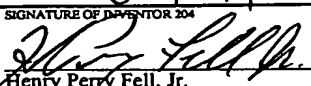
APPLICATION SERIAL NO.	FILING DATE	STATUS		
		PATENTED	PENDING	ABANDONED

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	POST OFFICE ADDRESS	STREET	CITY	STATE OR COUNTRY	ZIP CODE
206	FULL NAME OF INVENTOR	LAST NAME	FIRST NAME	MIDDLE NAME	
	RESIDENCE & CITIZENSHIP	CITY	STATE OR FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP	
	POST OFFICE ADDRESS	STREET	CITY	STATE OR COUNTRY	ZIP CODE

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

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DATE 6-7-99	DATE 6-7-99	DATE 6-7-99
SIGNATURE OF INVENTOR 204  Henry Perry Fell, Jr.	SIGNATURE OF INVENTOR 205	SIGNATURE OF INVENTOR 206
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